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ABSTRACT

Individuals who are intrinsically motivated to exercise are more likely to do so consistently. In previous research, those with at least one copy of the methionine (met) allele in the brain derived neurotrophic factor gene (BDNF; rs6265) had greater increases in positive mood and lower perceived exertion during exercise. This study examined whether genotype for BDNF is also related to intrinsic motivation, measured by self-report during a treadmill exercise session and a free-choice behavioral measure (continuing to exercise given the option to stop) among 89 regular exercisers (age M = 23.58, SD = 3.95). Those with at least one copy of the met allele reported greater increases in intrinsic motivation during exercise and were more likely to continue exercising when given the option to stop (55% vs. 33%). Results suggest that underlying genetic factors may partially influence perceptions of inherent rewards associated with exercise and might inform the development of individually targeted interventions.

Keywords: BDNF, val66met polymorphism, genetics, intrinsic motivation, exercise, humans

What Keeps a Body Moving? The Brain Derived Neurotrophic Factor val66met Polymorphism and Intrinsic Motivation to Exercise in Humans

Regular exercise can reduce the risk of developing chronic diseases associated with increased morbidity and mortality including cardiovascular disease, obesity, hypertension, and type 2 diabetes (Roberts & Barnard, 2005; WHO, 2008). Further, evidence suggests that regular exercise is related to better cognitive functioning (Hillman et al., 2008) and physical and mental well-being (Penedo & Dahn, 2005). Exercise has also been shown to be an effective treatment for mild to moderate depression (Carek et al., 2011; Dunn et al., 2005). However, physical activity levels[1] in the US are extremely low, with less than 5% of the adult population achieving recommended levels of objectively-measured activity (Troiano et al., 2008). Understanding the factors that underlie individual differences in exercise motivation and participation is crucial to the future of exercise promotion efforts.

Twin studies suggest that participation in leisure time physical activity has a significant heritable genetic component (e.g., Frederiksen & Christensen, 2003; Stubbe et al., 2006). Research examining the role of genetics in exercise is increasing dramatically (Rankinen et al., 2010), but much remains unclear about the specific genes associated with a more active phenotype, how to best utilize knowledge of genetics to increase exercise

[1]We consider physical activity as a global, generic term referring to all activities that have a raised level of energy expenditure above resting metabolic rate and includes incidental activity like walking to work and occupational physical activities as well as other non-sedentary behaviors. Exercise refers to formal, purposive activities with the goal of raising energy expenditure with a particular focus on improving health-related outcomes such as cardiovascular fitness or strength. In the current article, we mainly focus on exercise as a formal, purposive activity, but recognize that the literature on genetic correlates tends to focus on overall and leisure time physical activity.

through interventions, and if there are gene x environment interactions that lead some individuals to differentially benefit from exercise or suffer from being sedentary.

One difficulty in understanding the role of genetics in exercise is that it is a complex behavioral phenotype that is influenced by numerous genetic, physiological, psychological, and environmental factors. Recent commentaries have highlighted the importance of research that investigates the association between genes and factors upstream from the complex phenotypes frequently targeted in genetic research (e.g., physical activity or exercise, diet, body-mass index, depression). They note that a better understanding of the relationship between genetic factors and the psychological factors theoretically linked to health behavior changes can increase intervention efficacy, as it is the psychological factors that are often targeted in behavior change interventions (Bryan & Hutchison, 2012; McBride et al., 2012). For example, recent research has demonstrated that a candidate gene robustly associated with obesity, FTO (fat mass and obesity-associated), partially operates through increased energy intake that is associated with variability in perceptions of satiety (Hetherington & Cecil, 2010).

Furthermore, understanding how gene-environment interactions make an environment or behavior more harmful or beneficial for individuals with a certain genotype can be particularly useful. As a proof of concept, Phares et al. (2004) identified genotypic variations in adrenergic receptors that, in sedentary individuals, were associated with body fat distribution, obesity and/or altered lipolytic function, but when those individuals began an exercise intervention, they demonstrated greater *decreases* in all types of body fat relative to those without the genetic variations. Thus, a more clear understanding of how genes influence constructs theoretically and empirically related to

exercise and gene-exercise interactions can lead to more specifically tailored interventions targeted at those who can benefit the most from increased exercise. To that end, the current research aimed to examine whether variation in a single nucleotide polymorphism (SNP; val66Met) for the brain derived neurotrophic factor gene (BDNF; rs6265) that has been shown to influence mood response to exercise, was related to two measures of intrinsic motivation—a psychological construct theoretically and empirically linked to higher participation in exercise.

BDNF and Exercise

The val66met SNP is a common, functional polymorphism found in humans that results in a valine (val) to methionine (met) amino acid substitution at codon66. The BDNF gene controls expression of the BDNF peptide growth factor, which is associated with exercise in both humans (Cotman & Berchtold, 2002) and animals (Adlard et al., 2005). BDNF is known to regulate neuronal survival and plasticity, enhancing brain health, particularly in the hippocampus (Huang & Reichardt, 2001). Importantly, exercise has been shown to increase levels of BDNF (e.g., Adlard, et al., 2005; Ferris et al., 2007; Gómez-Pinilla et al., 2001). BDNF is also expressed in regions of the body relevant to physical activity, such as the spinal cord and skeletal muscle (Gómez-Pinilla, et al., 2001) and is implicated in the development of vasculature (Donovan et al., 2000).

Individuals with at least one copy of the met allele have been shown to have lower neuronal expression of BDNF (Chen et al., 2008), smaller hippocampal volume (e.g., Pezawas et al., 2004a), and impaired memory and hippocampal activation (Egan et al., 2003b). Interestingly, one study found that individuals with one copy of the met allele had a more positive mood response to a bout of moderate intensity exercise (65% of VO2max)

relative to those with a val/val genotype (Bryan et al., 2007). BDNF genotype has also been shown to moderate response to an exercise intervention (Bryan et al., 2013). In a randomized trial, those with the met allele in the intervention condition increased their aerobic exercise the most, while those with the met allele in the control condition exercised the least. This result is consistent with findings that the affective response to exercise influences future exercise motivation and participation (Kwan & Bryan, 2010a, 2010b; Williams et al., 2008; Williams et al., 2012). The purpose of the current study was to examine the association of variation in the val66met polymorphism with intrinsic motivation—a psychological construct that may play a role in translating the immediate emotional response to exercise into future exercise participation.

Intrinsic Motivation

Self-determination theory (SDT; Ryan & Deci, 2000) is a prominent multi-faceted theoretical approach that has received considerable empirical attention across a variety of behaviors (Deci et al., 1999). The basic tenets of this theory suggest that an individual's self-regulation of an action or behavior, defined as the successful initiation and maintenance of the behavior, is dependent on the quality rather than quantity of motivation experienced by the individual with respect to the behavior (for a comprehensive theoretical review see Ryan & Deci, 2000, 2007). Intrinsic motivation, the most self-regulated type of motivation, is defined as, "engaging in an activity for itself and for the *pleasure and satisfaction* derived from participation" (p. 427, Vallerand, 2004, emphasis added). Interventions utilizing SDT to increase exercise behavior have demonstrated some success (e.g., Chatzisarantis & Hagger, 2009; Fortier et al., 2007; Vansteenkiste et al., 2004). However, Ryan et al. (2008) acknowledged that "most health-

related behaviors, such as increasing physical activity, taking medications, or quitting smoking, are not intrinsically motivated or inherently enjoyable activities" (p. 3). While some people may not find exercise inherently enjoyable, there is evidence to suggest that many do, particularly those who are successful at maintaining a regular program of physical activity (e.g., Chatzisarantis et al., 2007; Ryan et al., 1997; Williams, et al., 2008). Moreover, experimentally-manipulated positive affect has been shown to increase intrinsic motivation for enjoyable activities, as well as activities that are not inherently enjoyable (Isen & Reeve, 2005).

The Current Study

Given that intrinsic motivation is related to both exercise participation and maintenance, and that there is evidence linking increased affective response to an activity and intrinsic motivation to engage in that activity, it is worth considering intrinsic motivation as an endophenotype that might be partially associated with genetic variation. Building on previous findings that exercise-induced positive mood/affect is related to variation in the val66met polymorphism in the BDNF gene, we sought to examine whether variation in the val66met polymorphism is related to intrinsic motivation to exercise, and test affective response as a mediator of this relationship. Individuals with the met allele have demonstrated a relatively more positive emotional response to exercise (Bryan et al., 2007); therefore we hypothesized that these individuals would also show greater intrinsic motivation (i.e., exercising for the enjoyment of participation) during a moderate bout of treadmill running. We further hypothesized that the relationship between genotype and intrinsic motivation would be mediated by affective response. Finally, in exploratory analyses, we aimed to further examine the relationship between affective response to

exercise and intrinsic motivation. We hypothesized that a positive affective response would be related to more intrinsic motivation for the laboratory exercise session, and general intrinsic motivation to exercise. Self-report measures were used to gauge situational intrinsic motivation and affect at three time-points during the exercise; and a free choice measure —choosing to continue running when given the option to stop—was used as an objective, behavioral proxy for intrinsic motivation (Deci, 1971; Hagger & Chatzisarantis, 2011).

Materials and Methods

Ninety-nine active, healthy individuals (45 women) between the ages of 18 and 35 (M = 23.57, SD = 3.97) volunteered for the study and were paid 25 USD for their participation. Participants were recruited from flyers placed around a University campus, and in coffee shops, restaurants, and exercise facilities around the Albuquerque metro area. Active was defined as voluntarily exercising 3 or more times per week for 30 minutes or more, verified by self-report in an initial screening interview conducted over the phone. All participants met the screening criteria of having healthy blood pressure (Systolic < 160 and Diastolic < 90) and Body Mass Index (18 < BMI < 30), and passed a physician screening. Participants were run individually. Ten participants did not provide adequate samples for DNA assay and were thus excluded from the analyses including genotype.

Following written informed consent, participants provided saliva samples for DNA assay and completed interview and questionnaire materials regarding current and previous exercise behavior. Participants were instructed to exercise on a treadmill at a self-defined moderate intensity, equivalent to a Rating of Perceived Exertion of 14 (RPE; Borg, 1998; Grant et al., 1999), for 30 minutes. Researchers asked participants questions

regarding the extent to which they were using certain motivation techniques and current affect at three time points during the exercise session (see "intrinsic motivation" and "affect" below). Prior to exercising, the in-task motivation and affect questions and the reporting technique were explained in detail to participants (for complete scale see Appendix in Online Supplemental Material). In order to limit socially desirable responses during exercise, cards were held up with each motivational technique or affect and response scale visible only to the participant. Researchers identified the items with a number, which was printed on the back of each card. Questions were asked in a random order within scale for each participant at each time point. The battery of questions took approximately two minutes to administer, and all questions were asked at approximately 8, 18, and 28 minutes into the session in order to complete the final battery before the 30 minutes of exercise was completed. After the exercise session participants completed a final battery of questionnaires that included the general intrinsic motivation to exercise measure.

The majority of the sample identified themselves as Caucasian (61%) and highly educated, with 12% having completed a Master's or higher degree, 41% having completed college or a 2-year vocational degree, and 44% having completed high school. This study was approved by the Human Research Review Committee at the University of New Mexico.

Measures

Exercise frequency and behavior. Overall level of physical activity was measured using the Stanford Seven-Day Physical Activity Recall (Blair et al., 1985; Sallis et al., 1985). This interviewer-administered survey was designed to calculate minutes of physical activity and total exertion including voluntary aerobic exercise, work-related activity, leisure-time

physical activity, and walking over the previous seven days. This measure is widely used in exercise research, and has demonstrated reliability and validity (Dishman et al., 2001; Pereira et al., 1997) and reasonable concurrent validity compared to activity measured by accelerometer (Sloane et al., 2009). From this interview we calculated individuals' minutes of moderate or higher intensity activity and days of exercise in the previous week. Participants also reported whether or not they performed different types of exercise (including running) in the previous 3 months.

Intrinsic motivation. Situational intrinsic motivation was measured in two ways. First, to specifically measure intrinsic motivation (i.e., pleasure and enjoyment) for the laboratory exercise, and measure changes over time in this motivation, participants were asked to rate how much had been thinking about 23 motivational techniques to help themselves work hard during the previous 10 minutes of exercise at three time-points during the 30-minute self-defined moderate intensity treadmill session (at approximately 8, 18, and 28 minutes). Cards with the motivational techniques and response scale were designed for participants to see easily while running, and maximize participants' privacy, as researchers could not see which question participants were answering. Each card included the question, "How much have you been thinking about…" and the motivational technique of interest. Three items adapted from the situational motivation scale were used to measure in-task intrinsic motivation to exercise (Guay et al., 2000; e.g., "How much are you thinking about the pleasure you are experiencing right now"). Responses ranged from 0 'not at all' to 4 'a lot' (average internal consistency for intrinsic motivation, $\alpha = .87$ across three time points). Random coefficient regression (see Kwan & Bryan, 2010b) was used to compute individual slopes of change in intrinsic motivation.

Second, a binary free-choice behavioral measure of intrinsic motivation was used to measure situational intrinsic motivation. Upon completing the mandatory 30-minutes of treadmill exercise, participants were given the option to continue exercising for 5-minutes or begin their cool down with the following prompt: "Your 30-minutes of exercise are complete. You now have a choice; you can either begin a 5-minute cool down or keep going at this pace for 5 more minutes and then begin your cool down. It's totally up to you." Choosing to continue constituted a behavioral indication of intrinsic motivation. Measuring free choice behavior is widely used as a proxy for intrinsic motivation and has been used specifically with exercise behavior (Cameron & Pierce, 1994; Deci, 1971; Deci, et al., 1999; Hagger & Chatzisarantis, 2011; Hagger et al., in press; Lonsdale et al., 2009; Patall et al., 2008).

Following the exercise, participants also completed a self-report measure to gauge intrinsic motivation to exercise more broadly with the Behavioral Regulations for Exercise Questionnaire-2 (BREQ-2; Markland & Tobin, 2004). The BREQ-2 is a widely used, validated 19-item scale designed to assess types of motivation from self-determination theory with respect to exercise. The BREQ-2 has five subscales measuring the levels of self-regulated motivations. For these analyses we used the subscale for intrinsic regulation of exercise behavior (internal consistency, $\alpha = .89$), and a composite measure, the Relative autonomy Index (RAI), that gauges more versus less self-regulated motivation to exercise. Each subscale is weighted accordingly to calculate the RAI for each participant (-3(amotivation) -2(external regulation) -1(introjected regulation) + 2(identified regulation) + 3(intrinsic regulation)). As per recommendations for using the RAI, we ensured that the

subscale scores conformed to a simplex pattern, with stronger positive correlations between adjacent than non-adjacent subscales.

Affective response. The feeling scale (FS), developed by Hardy and Rejeski (1989), is a single-item, 11-point dimensional measure of affect that corresponds with the valence component of Russell's (1980) circumplex model. It has been used as a measure of general affect during exercise and has shown reliability and discriminant validity from the RPE (Hardy & Rejeski, 1989). The physical activity affect scale (PAAS; Lox et al., 2000) was used to assess four additional dimensions of affective response to exercise. The 12-item PAAS has four subscales: positive affect ('enthusiastic', 'energetic', and 'upbeat'; average internal consistency $\alpha = .84$), negative affect ('miserable', 'discouraged', and 'crummy'; average internal consistency $\alpha = .76$), tranquility ('calm', 'relaxed', and 'peaceful'; average internal consistency $\alpha = .82$) and fatigue ('fatigued', 'tired', and 'worn-out'; average internal consistency $\alpha = .84$). Participants rated their current affective state for each item on a scale from 0 'do not feel' to 4 'feel very strongly'. Individual slopes of change in affective valence and each subscale of the PAAS during exercise were computed to test whether affective response mediated the relationship between BDNF and intrinsic motivation, and examine the relationships between affective response and intrinsic motivation.

Exercise intensity. To measure the intensity of participants' exercise during the self-defined moderate exercise, average speed was calculated from the distance and time recorded on the treadmill at the completion of the 30 minutes of exercise and heart rate was measured using a Timex Digital heart rate monitor (Middlebury, CT) at each timepoint. Slopes of heart rate increase were computed for each participant using random coefficient regression.

DNA. Saliva was collected and the candidate BDNF gene was analyzed following published procedures (see Freeman et al., 1997; Walker et al., 1999). Participants were instructed to generate and deliver 5 ml of saliva into a sterile 50 ml conical centrifuge tube. The saliva sample was then placed in the refrigerator and lysis buffer was added within 24 hours. Tris-HCl (pH 8), EDTA (pH 8), SDS and NaCl were added at 100 mM, 20 mM, 0.5% and 125 mM final concentrations, respectively. The tubes were refrigerated until the DNA was extracted, usually within 48 hours. Proteinase K (0.2 mg/ml) was added and the tubes were incubated at 65°C for 60 minutes. An equal volume of isopropyl alcohol was then added to each tube, the contents were mixed, and the DNA was collected by centrifugation at 3,500 x g for 10 minutes. The DNA pellet was rinsed once with one ml of 50% isopropyl alcohol and allowed to air dry. For RNase treatment, 20 ug/ml RNAse A and 50 U/ml RNase T1 were added and incubated at 37°C for 30 minutes. To precipitate the DNA, two volumes of 95% ethanol were added and mixed by gentle inversion, and then collected by centrifugation at 3,500 x g for 15 minutes. The samples were allowed to air dry followed by re-suspension in 1 ml of 10 mM Tris-HCl, 10 mM EDTA buffer (pH 8.0), and placed in a 1.8 ml cryovial. The concentration of DNA was calculated from the absorbance at 260 nm analysis and then adjusted to a concentration of 10 ng/μL. Samples were genotyped using TaqMan® primer and probe pairs; the probes were conjugated to two different dyes (one for each allelic variant). Taqman assays were designed and selected using the SNPBrowser™ program (Applied Biosystems) and ordered directly from this company. The PCR reaction mixture consisted of 20 ng of genomic DNA, 1× Universal PCR Master Mix, 900 nM of each primer and 200 nM of each probe in a 15 μL reaction volume. Amplification was performed using the TaqMan® Universal Thermal Cycling Protocol and fluorescence

intensity was measured using the ABI Prism 7500 Real-Time PCR System. Genotypes were acquired using the 7500 system's allelic discrimination software (SDS version 1.2.3). The genotype frequencies for the rs6265 polymorphism were 67% val/val (n = 60), 29% val/met (n = 26), and 3% met/met (n = 3), which were in Hardy-Weinberg equilibrium (p = .59) with an overall minor allele frequency of .19 (see Table 1). These frequencies are consistent with expected population rates and previously reported distributions (Gatt et al., 2009 Molecular Psychiatry; Egan et al., 2003, Cell: Lang et al., 2004; Jiang et al., 2005). Due to the small number of participants with the met/met genotype, we collapsed across those with at least one copy of the met allele for between group comparisons as has been done in prior work (e.g., Bryan, et al., 2007; Bryan, et al., 2013; Gatt et al., 2009; Hariri et al., 2003; Jiang et al., 2013) and as is consistent with research on the BDNF SNP more broadly (Anastasia et al., 2013; Egan et al., 2003a; Kleim et al., 2006; Pezawas et al., 2004b; Szeszko et al., 2005).

Results

Preliminary analyses

We tested for differences between those with a met allele and those with a val/val genotype, and differences between those who continued to exercise and those who did not in potentially confounding variables and to provide evidence of construct validity of the behavioral measure using a series of non-parametric Mann-Whitney tests on the continuous variables of interest[2], and Fisher's exact tests for dichotomous variables. Effect sizes for Mann-Whitney tests were computed as described by Field (2009) for significant differences between groups ($r = Z/\sqrt{N}$). We first tested for differences in the genotype

[2] Non-parametric tests were used because several of the dependent measures were not normally distributed in the current sample.

groups in age, body mass index (BMI), and blood pressure (Table 1). No differences were found between those with a met allele and those with a val/val genotype. Next, we tested that the groups did not differ on current exercise behavior or exercise intensity during the laboratory exercise session (Table 2). There were no differences between genotype groups or between those who continued and those who did not in minutes or days of exercise in the previous week, frequency of participants who reported running for exercise, heart rate response or average speed during the laboratory controlled exercise session.

Situational intrinsic motivation averaged across timepoints during the laboratory exercise was significantly greater for those who continued to exercise (*Mdn* = 2.67) than for those who did not (*Mdn* = 2.22), $U = 893.5$, $p < 0.05$, $r = 0.20$; as was general intrinsic motivation to exercise (*Mdn* = 3.75 vs. *Mdn* = 3.25 respectively), $U = 876.00$, $p = 0.03$, $r = 0.22$; and the relative autonomy index of self-regulated motivation for exercise (*Mdn* = 14.42 vs. *Mdn* = 12.75 respectively), $U = 781$, $p = 0.02$, $r = 0.25$. Thus, continuing to exercise was clearly related to self-reported measures of intrinsic motivation and can be considered a reasonable proxy for intrinsic motivation in the current study.

BDNF and self-report intrinsic motivation during exercise

To examine change over time in self-reported situational intrinsic motivation, we fit a multilevel growth curve model with intrinsic motivation at each of the three time-points (level-1) nested within each individual (level-2). Time was centered at the first time-point to allow for a meaningful interpretation of the intercept. BDNF genotype (met/met or val/met vs. val/val) was entered as a level-2 predictor. Time was entered as a random effect to allow individual slopes and intercepts to vary. We included a BDNF X time interaction to test for a moderating effect of BDNF on changes over time in intrinsic

motivation. To control for individual differences in exercise frequency, exercise frequency (mins/week) was included as a level-2 covariate. Overall, there was no significant linear effect of time on intrinsic motivation, β = -0.01, *SE* = 0.06, p = 0.86, indicating that, on average, individuals did not demonstrate significant changes in intrinsic motivation across the exercise bout. There was also no main effect of BDNF on intrinsic motivation β = -0.20, *SE* = 0.21, p = 0.35, meaning that when averaging across timepoints, there were no differences in intrinsic motivation between genotype groups. ANOVA components indicated significant variability in both the intercept and slope of change in intrinsic motivation (*p's* < 0.01), but there was no relationship between the intercept and slope (p = 0.84). Thus, participants varied significantly in their initial rating of intrinsic motivation and in the pattern of ratings of intrinsic motivation over time, but participant's initial rating of intrinsic motivation was not related to change in motivation over time. Importantly, a significant BDNF X time interaction was observed, $F(1, 87) = 4.87$, p = 0.03, indicating that differences in intrinsic motivation over time were significantly different between those with a met allele and those with a val/val genotype. We further probed this interaction to test the direction of the relationship. Intrinsic motivation increased significantly over time for those with a met allele (p = 0.01) but did not change for individuals with a homozygous val genotype (p = 0.86; see Figure 1).

BDNF and self-reported affect during exercise

To examine change over time in self-reported affective valence and positive affect, we fit similar multilevel growth curve models for each variable at all three time-points (level-1) nested within each individual (level 2). Again, time was centered at the first time-point to allow for a meaningful interpretation of the intercept. BDNF genotype (met/met or

val/met vs. val/val) was entered as a level-2 predictor. Time was entered as a random effect to allow individual slopes and intercepts to vary. We included a BDNF X time interaction to test for a moderating effect of BDNF on changes over time in the affective variables. To control for individual differences in exercise frequency, exercise frequency (mins/week) was included as a level-2 covariate. Overall, there was no significant linear effect of time on positive affect, $\beta = 0.03$, $SE = 0.05$, $p = 0.53$, indicating that, on average, individuals did not demonstrate significant changes in positive affect across the exercise session. There was also no main effect of BDNF on positive affect $\beta = -0.10$, $SE = 0.17$, $p = 0.58$, meaning that when averaging across timepoints, there were no differences in positive affect between genotype groups. ANOVA components indicated significant variability in both the intercept ($p < 0.01$) and slope of change in positive affect ($p = 0.02$), but there was no relationship between the intercept and slope ($p = 0.66$). Thus, participants varied significantly in their initial rating of positive affect and the pattern of positive affect over time, but participant's initial rating was not related to change in positive affect over time. There was not a significant BDNF X time interaction, indicating that differences in positive affect over time were not different between those with a met allele and those with a val/val genotype.

Overall, there was a significant linear effect of time on affective valence, $\beta = 0.22$, $SE = 0.08$, $p < 0.01$, indicating that, on average, individuals demonstrated significant increases in affective valence across the exercise session. There was no main effect of BDNF on affective valence, $\beta = -0.47$, $SE = 0.29$, $p = 0.11$, meaning that when averaging across timepoints, there were no differences in affective valence between genotype groups. ANOVA components indicated significant variability in both the intercept and slope of

change in positive affect (p's < 0.01), but there was no relationship between the intercept and slope (p = 0.72). Thus, participants varied significantly in their initial rating of affective valence and the pattern of affective valence over time, but initial ratings were not related to change in affective valence over time. As with positive affect, the BDNF X time interaction was not significant (p = 0.76), indicating that differences in affective valence over time were not different between those with a met allele and those with a val/val genotype.

Free-choice behavioral measure of intrinsic motivation

Overall, 40% of participants continued to exercise when given the option to stop. Among those with a met allele, over half (55%) kept going, while just 33% of those with a val/val genotype kept going. We used logistic regression to determine the odds ratio for choosing to continue exercising when given the option to stop, controlling for current exercise behavior (mins/week). The odds of continuing were significantly greater for those with a met allele (OR = 2.58 [95 % CI: 1.03-6.46], p = .04; see Figure 2). Next, we tested the effect of BDNF genotype on continuing to exercise controlling for exercise frequency and affective valence at time 3, just prior to choosing whether or not to continue exercising. The magnitude of the effect of BDNF genotype increased when including affective valence (OR = 3.78 [95% CI: 1.35- 10.60], p = .01). Affective valence at time 3 was independently related to choosing to continue exercising (OR = 1.89 [95% CI: 1.27- 2.83], p < .01).

Mediation of the BDNF-intrinsic motivation relationship by affective response

In the current study, BDNF genotype was not related to positive affect or affective valence response to exercise. We were thus unable to test affective response as a mediator of the relationship between BDNF and intrinsic motivation.

Exploratory analyses: Self-reported affective and motivation response by BDNF and free choice behavior

Consistent with the results from the growth curve analyses, Mann-Whitney tests revealed that those with a met allele had greater increases in intrinsic motivation (*Mdn* = 0.17) compared to those with a val/val genotype (*Mdn* = 0.00), $U = 646.50$, $p = 0.05$, $r = 0.20$. No differences were found in affective valence, positive affective, negative affective, tranquility, or exhaustion response to the exercise session, or in general intrinsic or self-regulated motivation for exercise out of the context of exercise (all results are summarized in Table 2). Those who continued to exercise reported greater increases in affective valence (*Mdn* = 0.50) than those who chose not to (*Mdn* = 0.00), $U = 847.50$, $p = 0.02$, $r = 0.24$, greater increases in positive affect (*Mdn* = 0.17) than those who chose not to (*Mdn* = 0.00), $U = 835.00$, $p = 0.02$, $r = 0.24$, and greater increases in tranquility during exercise (*Mdn* = 0.00) than those who chose not to continue (*Mdn* = 0.00), $U = 889.00$, $p = 0.04$, $r = 0.20$. There were no significant differences between those who chose to continue and those who did not in intrinsic motivation response, or negative affective or exhaustion response.

Correlations between the motivation and affective response variables and general intrinsic motivation and relative autonomy index are in Table 3. Notably, general intrinsic motivation was correlated with intrinsic response to the exercise session ($r = 0.27$, $p < 0.01$), affective valence response ($r = 0.29$, $p < 0.01$), positive affective response ($r = 0.24$, $p < 0.01$), and inversely correlated with negative affective response ($r = -0.27$, $p < 0.01$).

Discussion

The aim of this study was to examine whether the val66met polymorphism in the BDNF gene was associated with situational intrinsic motivation (i.e., exercising for the

enjoyment of participation) during a moderate intensity bout of treadmill running. We further aimed to test affective response as a mediator of this relationship, and examine the relationship between affective response to an exercise session and intrinsic motivation to exercise. Results demonstrated an association between the BDNF SNP and two measures of situational intrinsic motivation: changes in self-reported intrinsic motivation during the exercise session, and a free choice behavioral measure, continuing to participate when given the option to stop. Those with at least one copy of the met allele showed significant increases in self-reported intrinsic motivation during the bout of exercise, and were significantly more likely to continue exercising after being given the option to stop. The odds of continuing among those with at least one copy of the met allele were more than 2.5 times larger than the odds among individuals with a val/val genotype. Contrary to expectations, there were no differences between genoytype groups in general intrinsic motivation to exercise measured after the exercise task; thus the association between the SNP and intrinsic motivation seems to require the presence of the specific reinforcing activity (exercise). In the current study, BDNF genotype was not related to affective valence or positive affective response; the hypothesis that affective response mediates the relationship between BDNF and intrinsic motivation was therefore not supported.

These results make a novel contribution to the literature on factors that underpin individual differences in exercise motivation. A greater understanding of these factors can ultimately lead to more effective, individualized interventions to initiate and maintain healthy exercise patterns. If health promoters are able to use genetic and other individual difference variables to identify individuals who have a heritable tendency to enjoy exercise less, and are likely to be less intrinsically motivated during exercise, more intensive

interventions can be developed and implemented in order to help those individuals initiate and maintain exercise behavior. Our findings suggest that those with a met allele for the val66met polymorphism experience increases in finding exercise enjoyable or pleasurable as a single session goes on, and are more likely to want to persist running in the absence of external rewards or commitments. For these individuals, exercise itself, or intervention materials focused on how pleasurable exercise is, may be more likely to motivate maintenance of exercise behavior. On the other hand, individuals with a val/val genotype may benefit more from intervention materials focused on other, more extrinsic, motivational incentives or benefits of exercise such as rewards or losing weight (Hagger et al., 2014).

While the mechanism that would lead those with a met allele to have a more pleasurable response to exercise and choose to continue exercising remains unclear, a number of pathways indicated by previous research may be relevant. First, BDNF is synthesized in areas of the brain associated with reward processing (Seroogy et al., 1994). Recall that individuals with at least one copy of the met allele have lower neuronal expression of BDNF (Chen, et al., 2008) and impaired hippocampal activation (Egan, et al., 2003b), and that exercise increases BDNF (e.g., Adlard, et al., 2005; Ferris, et al., 2007; Gómez-Pinilla, et al., 2001). The met allele may therefore alter sensitivity and/or response to a rewarding stimulus (i.e., exercise), due to differences in baseline BDNF, differences in neurocognitive structure, or differences in exercise induced increases in BDNF. This type of mechanism has been suggested to understand evidence that those with the met allele are more likely to smoke cigarettes or have addictive vulnerability to substances that increase BDNF levels (Lang et al., 2007).

Exercise induced increases in BDNF secretion in the brain may lead to a relatively greater pleasurable response to exercise among individuals with the met allele, which was reflected by increases in the use of intrinsic motivation and choosing to continue exercising when given the option to stop. Notably, however, we did not find evidence that the relationship between BDNF genotype and the behavioral measure of intrinsic motivation is mediated by affective valence or positive affective response during the exercise, as BDNF genotype was not related to affective response in the current study. This finding is inconsistent with the results of Bryan et al. (2007), who found that those with a met allele had a greater positive affective response to exercise. This may be due to a key methodological difference; in the Bryan et al. study, exercise intensity was objectively controlled (at 65% of individual's predetermined VO_2max), whereas participants in the current study chose the pace they felt was of a moderate intensity. This self-defined moderate intensity may have been a rate at which they were more likely to feel positive and less likely to feel negative affect overall, or resulted in less variation in positive affect in the current study. It may also simply be the case that affect is not the factor that mediates BDNF genotype and the behavioral measure of intrinsic motivation. Despite the methodological differences, those with the met allele demonstrated increases in utilizing how pleasurable and enjoyable the exercise was to stay motivated during exercise, which our results suggest is distinct from affective valence and positive affective response to the exercise session. Interestingly, in a study examining potential physiological and psychological moderators of an exercise intervention, BDNF genotype, but not affective response, moderated the effect of intervention on exercise behavior over a 12-month follow-up period (Bryan et al., 2013). Those with a met allele in the intervention condition

exercised the most, while those with a met allele in the control condition exercised the least.

Our results suggest that affective valence and positive affective response are related to intrinsic motivation measured during exercise, the decision of whether or not to continue exercising, and general intrinsic motivation for exercise. A one unit increase in positive affect at the end of the exercise session nearly doubled the likelihood of choosing to continue exercising, independent of the effect of BDNF. Paradoxically, those who continued running did not have significantly greater increases in intrinsic motivation to exercise compared to those who chose to stop running. There is clearly a connection between affective response and intrinsic motivation, but our results suggest that neither responses in affective valence or positive affect, nor responses in intrinsic motivation during an exercise session, mediated the relationship between BDNF and the behavioral measure of intrinsic motivation.

Relationships between BDNF, depression, and exercise may provide another potential mechanism through which BDNF genotype results in differences in intrinsic motivation during exercise and the behavioral measure of intrinsic motivation. BDNF has been recognized as one of the best candidate molecules for understanding the antidepressant effects of exercise (C. H. Duman et al., 2008; Heyman et al., 2012; Li et al., 2008), particularly by promoting neurogenesis (Erickson et al., 2011; Heyman, et al., 2012; Lafenetre et al., 2010). Though typically only thought of for its role in memory, hippocampal neurogenesis likely plays a role in the behavioral effects of antidepressants (Sahay & Hen, 2007) and common antidepressant drugs increase hippocampal neurogenesis (Malberg et al., 2000). The relationship between hippocampal neurogenesis

and perceptions of enjoyment/pleasure is not well understood, but it is potentially involved with immediate emotional response to exercise (Becker & Wojtowicz, 2007), which was reflected in self-reported use of intrinsic motivation measured *during* exercise.

Moreover, low levels of BDNF are associated with increased risk of depression (e.g., R. S. Duman & Monteggia, 2006; Karege et al., 2002). While some studies have found that individuals with a met allele are more likely to suffer from depressive symptoms, the findings are inconsistent (reviewed in Levinson, 2006). One potential explanation for these inconsistencies is that there are gene-environment interactions that influence complex phenotypic outcomes like depression. One study found that the BDNF SNP moderated the relationship between exercise and depressive symptoms such that those with the met allele were *less* likely to experience depressive symptoms if they were active, but *more* likely to experience depressive symptoms if sedentary (Mata et al., 2010; but see Stavrakakis et al., 2012 for failure to replicate). Taken together with the current results, the findings of Mata et al. suggest that not only are those with a met allele more likely to be more motivated to continue based on the pleasure and enjoyment they experience during exercise, there may also be gene-exercise interactions that result in greater mental health outcomes when active, and more detrimental outcomes when sedentary. Carriers of the met allele may thus be particularly important to target for an exercise intervention intended to increase positive mental health outcomes through increased exercise.

It should be noted that, due to facility limitations and safety concerns, we were not able to leave participants alone during the free-choice period. We could therefore not unequivocally rule out the possibility that participants continued to exercise out of obligation to the experimenter, an extrinsic motivation. The significant relationships

between free-choice exercise and general and in-task intrinsic motivation seem to mitigate against this possibility, however. In addition, participants in this study were regular exercisers and only exercised on a treadmill during the study. Therefore, our results may not generalize to sedentary individuals or across all types of exercise. Future research should examine the val66met polymorphism and intrinsic motivation for other types of exercise and among less active or sedentary people.

Despite these limitations, the results of this study suggest that the experience of, and the motivation to, engage in moderate intensity exercise are associated with variation in the val66met polymorphism for the BDNF gene. From a broader perspective, the current results contribute to the exploration of a range of genetic, psychological, and environmental factors that interact to influence the enjoyment of, and intrinsic motivation to, engage in exercise. A better understanding of these factors is crucial to the development of more effective, tailored interventions targeted at those who can benefit the most from exercise.

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Figure 1. Changes in self-reported intrinsic motivation during exercise. Those with a met allele demonstrated significant increases in intrinsic motivation ($p < .05$).

Figure 2. Proportion of individuals who chose to continue exercising 5 more minutes given the option to stop by genotype. Significantly more individuals with one copy of the met allele demonstrated free-choice intrinsic motivation.